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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/171,916	02/16/99	NAIR	S 1579-312

EXAMINER	
GUZO,D	
ART UNIT	**PAPER NUMBER**
1636	11

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DATE MAILED: 02/21/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/171,916	NAIR ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 October 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

Double Patenting

Claims 1-8,13, 25-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 5,853,719. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims differ only in the terminology used to describe the source of the RNA isolated from the tumor. In the instant case applicants recite introducing into an APC "...tumor derived RNA..." while the claims in the '719 patent recite introducing into the APC "...RNA obtained from a tumor..." Since the most obvious way of deriving RNA from a tumor cell would be to obtain it from a tumor cell, it must be considered that the ordinary skilled artisan would derive RNA from a tumor cell by merely obtaining the RNA from a tumor cell. The ordinary skilled artisan would have been motivated to derive RNA from a tumor cell by obtaining the RNA from the cell because the obvious source of RNA from a tumor cell is the tumor cell itself. Given the teachings of the claims in the '719 patent and the level of skill in the art at the time the invention was made, it must be considered that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 19 and 42 rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim reads on a CTL claimed in a product by process context. The claimed process for producing the CTL would generate a CTL cytotoxic for the given tumor cell antigen(s) presented by the APC. Since a CTL cytotoxic for the same tumor can be produced naturally in a patient *in vivo*, it must be considered that the claimed CTL reads on a product of nature.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> **A person shall be entitled to a patent unless –**
>
> **(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.**

Claims 20-24 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Hellstrom et al.

Applicants claim a method for treating cancer or pathogen infection in a patient, said method comprising administering to said patient a therapeutically effective amount of a CTL cytotoxic for a target tumor cell or a target cell infected with a pathogen. The CTL is generated by contacting a lymphocyte in vitro with an APC of the instant invention.

Hellstrom et al. (U.S. patent 4,918,164, issued 4/17/90, see whole document, particularly columns 5, 25-26, etc.) recites a method for treating cancer or viral infected cells expressing viral induced tumor antigens in a patient, said method comprising administering to said patient a therapeutically effective amount of a CTL cytotoxic for a

target tumor cell or a target cell infected with a pathogen. Since the CTLs generated by the methods of the Hellstrom et al. are functionally identical (absent evidence to the contrary) to the those recited in the claims (i.e. they are cytotoxic for target tumor or pathogen infected cells in the patient), it must be considered that Hellstrom et al. teaches the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> **A person shall be entitled to a patent unless –**
>
> **(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.**

Claims 20-24 and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Kubo et al. or Srivastava et al.

The claimed invention is as described in the above 35 USC 102(b) rejection of claims 20-24 and 43.

Kubo et al. (U.S. Patent 5,662,907, issued 9/2/97, field 1/25/94, see whole document, particularly Columns 2, 4, 12 and 17) and Srivastava et al. (U.S. Patent 6,130,087, issued 10/10/00, filed 10/7/96, see whole document, particularly columns 3-5, 10-11) recite methods of treating cancer or pathogen infection comprising administering to patients CTLs generated in vitro and cytotoxic to target tumor cells or pathogen infected cells. Therefore, Kubo et al. and Srivastava et al. teach the claimed invention.

Claim R jections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 14-17, 20-24 and 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating cancer or pathogen infection in patients, does not reasonably provide enablement for preventing cancer or pathogen infection in patients. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants claim a method for preventing tumor formation in a patient comprising administrating to the patient a therapeutically effective amount of a tumor RNA-loaded APC or an effective amount of CTLs produced by contacting T lymphocytes with tumor RNA loaded APCs *in vitro*. Applicants also claim a method for preventing pathogen infection in a patient comprising administering to the patient a therapeutically effective amount of the CTL produced by contacting T lymphocytes *in vitro* with APCs loaded with pathogen-derived RNA.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics.*, 8 USPQ2d 1217 (Fed. Cir. 1988). Whether experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These

factors were outlined in *In re Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986 and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and they include the following: 1) Unpredictability of the art. The art in the area of cancer vaccines and gene therapy related vaccines against infectious diseases is highly unpredictable. With regard to recombinant based cancer vaccines, Gomez-Navarro et al. (European Journal of Cancer, 1999, Vol. 35, No. 6, pp. 867-885) note that the human immune system "...requires a complex network of balances and counterbalances to control the pathways of activation and termination of the immune response. Interventions directed to supplement or inhibit single mediators will most probably yield partial physiological and therapeutic results in the best case, may frequently yield no result at all, and occasionally will produce effects opposed to those desired." (Gomez-Navarro et al., pp. 874-875). Also, since most animal model studies on the efficacy of cancer vaccines and treatments involve human xenografts, it is unclear whether said vaccines and treatments would be efficacious against naturally occurring or spontaneously forming tumors in the host animal or in humans (See for example; Morel et al., Cancer Gene Therapy, 1998, Vol. 5, No. 2, pp. 92-100). It is also noted that use of human xenograft models in mice are generally unpredictable with regard to identification of anti-cancer drugs or treatments which would be effective in humans (See Gura, Science, 1997, Vol. 278, pp. 1041-1042). It is also noted that a major problem with tumor vaccines or treatments involves the development of antigen loss variants involving loss of the target antigen from cancer cells, down-regulation or loss of β_2-microglobin or MHC class I molecules or genetic defects in the MHC class I antigen presentation machinery that

can prevent effective CTL recognition of the target. Additionally, tumors may secrete immunosuppressive factors or factors which may induce T-cell apoptosis, etc. (See Pardoll, Nature Medicine, 1998, Vol. 4, No. 5, pp. 525-531). All of these factors contribute to the unpredictability of the art in this field.

With regard to recombinant vaccines or treatments for pathogens in humans, it is noted that the art is extremely unpredictable (See Cohen, Science, 1994, Vol. 265, pp. 1371-1371; Sprent et al., Science, 1994, Vol. 265, pp. 1395-1399; Rabinovich et al., Science, 1994, Vol. 265, pp. 1401-1404, etc.). Given that the instant claims are broad (reading on vaccines against any pathogen), given that different pathogens have different strategies for evading the host immune system (See Oldstone, Virology, 1997, Vol. 234, pp. 179-185), given that protective immunity against many pathogens must be at the site of infection of the pathogen (i.e. mucosal immunity is essential in any vaccines against poliovirus infection), given that many pathogens avoid the host immune system by residing at sites in the body (i.e. HIV particles that persist in lymph nodes) that are relatively inaccessible to conventional treatments or vaccines and given that many pathogens can present different antigenic epitopes to the host immune system over time (i.e. HIV, malaria, trypanosomes, etc.), the skilled artisan would conclude that it would be unpredictable as to whether the administration of CTLs generated by contacting T-lymphocytes with APCs of the instant invention would be effective as vaccines against diseases such as AIDS, HCV infection, malaria, etc.

2) State of the art. The state of the art at the time of applicants' invention was nil with no examples of successful cancer vaccines or CTL based vaccines against infectious disease using RNA-loaded APCs or CTLs generated from contact with said APCs.

3) Number of working examples. Applicants present no working examples of the claimed invention.

4) Amount of guidance presented by applicants. Applicants present some data involving mouse models which do not involve naturally occurring tumors or spontaneously occurring tumors and it is unclear what relevance this data would have for treatment or vaccination of humans against naturally occurring tumors.

5) Scope of the claims. The claims are very broad and read on prevention or treatment of any of the thousands of different types of cancer or any of the thousands of different pathogens which infect humans.

6) Nature of the invention. The invention involves one of the most complex areas of medicine/molecular biology; recombinant gene therapy methods to prevent or treat any cancers or any infectious disease.

7) Level of skill in the art. The level of skill in the art is high; however, given the level of unpredictability of the art, the poorly developed state of the art, the lack of guidance presented by applicants and the broad scope of the invention, it must be considered that the skilled artisan would have needed to have practiced undue and excessive experimentation in order to practice the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be concluded that the

skilled artisan would have had to have conducted undue and excessive experimentation in order to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 9, 33, 37 and 39 (and dependent claims) are vague in the use of the terms "...tumor-derived RNA..." (in Claim 1) or "...pathogen-derived RNA..." (in Claim 33) because it is unclear what is meant by the term "derived", i.e. does this term imply some undisclosed modification of the RNAs "derived" from the tumor or pathogen or does it read on simply obtaining the RNAs from the recited sources? The metes and bounds of the claimed subject matter are unclear.

Claim 43 is vague in that the claim recites a method for treating or preventing pathogen infection in a patient, comprising administering to the patient a therapeutically effective amount of the CTLs produced by the method of claim 41. However, claim 41 recites a method for generating CTLS cytotoxic for cells presenting a tumor antigen. It is unclear how the CTLs specific for tumor antigen presenting cells can be used for treating or preventing pathogen infection in patients.

Claim 51 (and dependent claims) are vague in that applicants recite administering a "therapeutically effective" amount of RNA loaded APCs in the context of a method for

detecting an increas in tumor-specific or pathogen specific CTL in a patient. It is unclear what condition the "therapeutically effective" amount of APCs is directed against, i.e. if the person does not have the tumor or pathogen, what is a therapeutically effective amount of the APC?

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding or relating to attachments to this Office Action should be directed to Patent Analyst Zeta Adams whose telephone number is (703) 305-3291.

David Guzo
February 16, 2001

DAVID GUZO
PRIMARY EXAMINER